

Protecting Children: Influenza Updates for Clinicians

**Clinician Outreach and
Communication Activity (COCA)
Webinar
February 26, 2015**

Objectives

At the conclusion of this session, the participant will be able to:

- ❑ **Describe strategies to assist clinicians in caring for children for the remainder of the 2014-2015 influenza season**
- ❑ **Identify approaches and emphasize the value for using antiviral therapy in children**
- ❑ **Discuss ways to encourage continued vaccination despite the drifted influenza A (H3N2) viruses**

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TODAY'S PRESENTERS



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TODAY'S PRESENTERS



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Influenza Vaccination Still Matters



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SCHOOL of MEDICINE**
AT HOFSTRA UNIVERSITY

Take Home Messages

- **Influenza H3N2 is the predominant strain; majority are drifted strains.**
- **Vaccine effectiveness may vary by match/mismatch of circulating virus with vaccine strains, vaccine product, and age of patient.**
- **Continue giving any licensed and age-appropriate influenza vaccine available; never delay for a specific product.**
- **Healthy children ages 2 through 8 years may be immunized with either IIV or LAIV (no preference).**

Estimated Vaccine-Preventable Disease Incidence and Deaths in the US

Disease	Annual Cases	Annual Deaths
Influenza ^{a,b}	61,000,000 ^c ('09)	3,349–48,614 ('76– '07)
Pneumococcal disease, invasive (bacteremia & meningitis) ^d	42,000 ('07)	4,500 ('07)
HPV ^e (cervical cancer)	10,520 ('04)	3,900 ('04)
Hepatitis B ^f	4,519 ('07)	719 ('07)
Meningococcal disease ^f	1,077 ('07)	87 ('07)
Hepatitis A ^f	2,979 ('07)	34 ('07)
Varicella ^f (chickenpox)	40,146 ('07)	14 ('07)
Pertussis ^f	10,454 ('07)	9 ('07)

^a CDC. Updated CDC Estimates of 2009 H1N1 Influenza Cases, Hospitalizations, and Deaths in the US. April 2009 – April 10, 2010. Available at [cdc.gov/h1n1flu/estimates\)2009_h1n1.htm](http://cdc.gov/h1n1flu/estimates)2009_h1n1.htm).

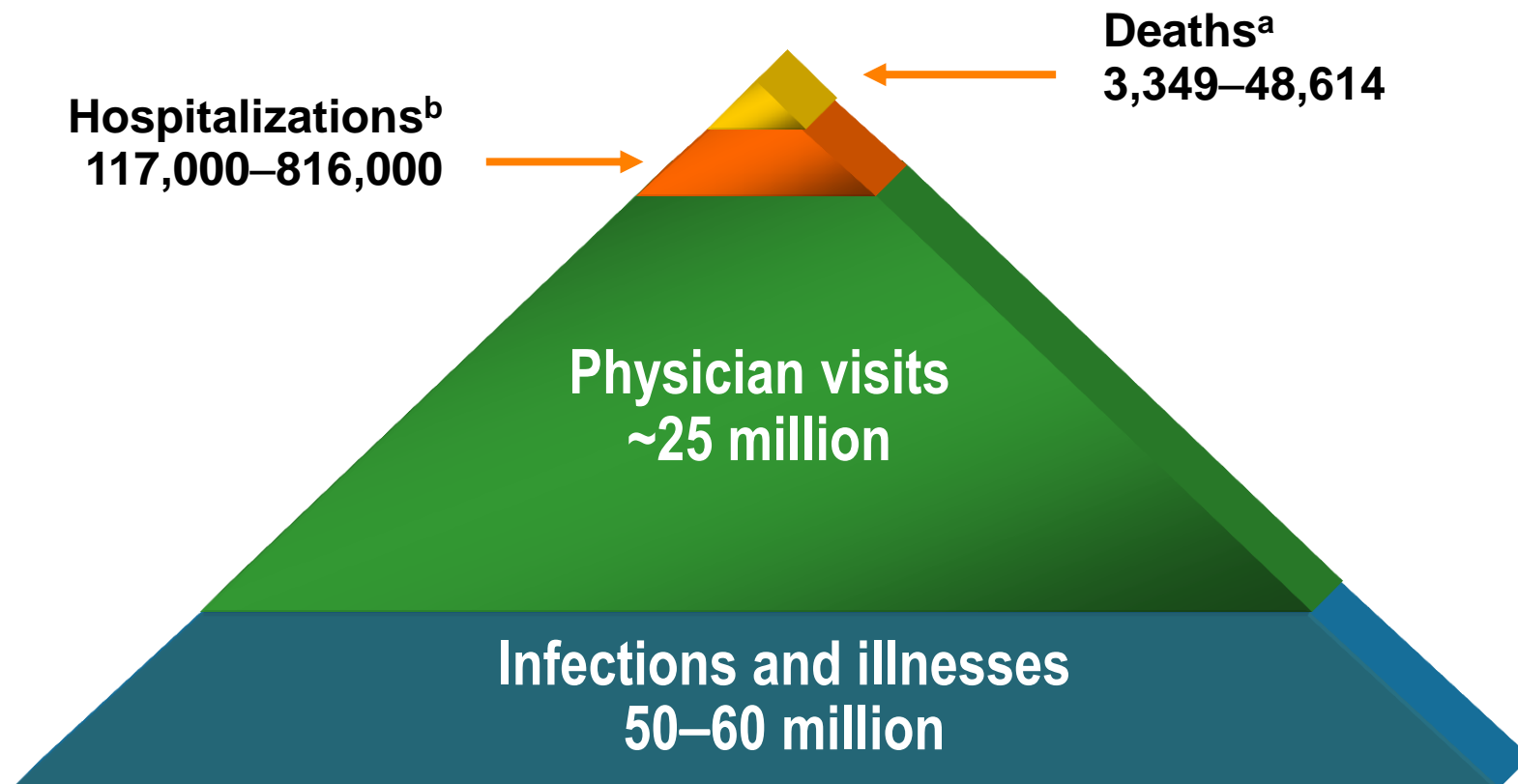
^b MMWR. 2010; 59 (22): 1057-62. ^c Data based on CDC estimates of 2009 H1N1 cases using statistical modeling.

^d CDC. ABCs Report: *Streptococcus pneumoniae*, 2007. Available at <http://www.cdc.gov/abcs/reports-findings/survreports/spneu04.html>.

^e American Cancer Society. Cancer Facts and Figures 2004. Available at cancer.org/downloads/STT/CAFF_finalPWSecured.pdf.

^f CDC. *Pink Book*. 12th ed. Available at <http://www.cdc.gov/vaccines/pubs/pinkbook/default.htm>.

Influenza Disease Burden in the US in an Average Year

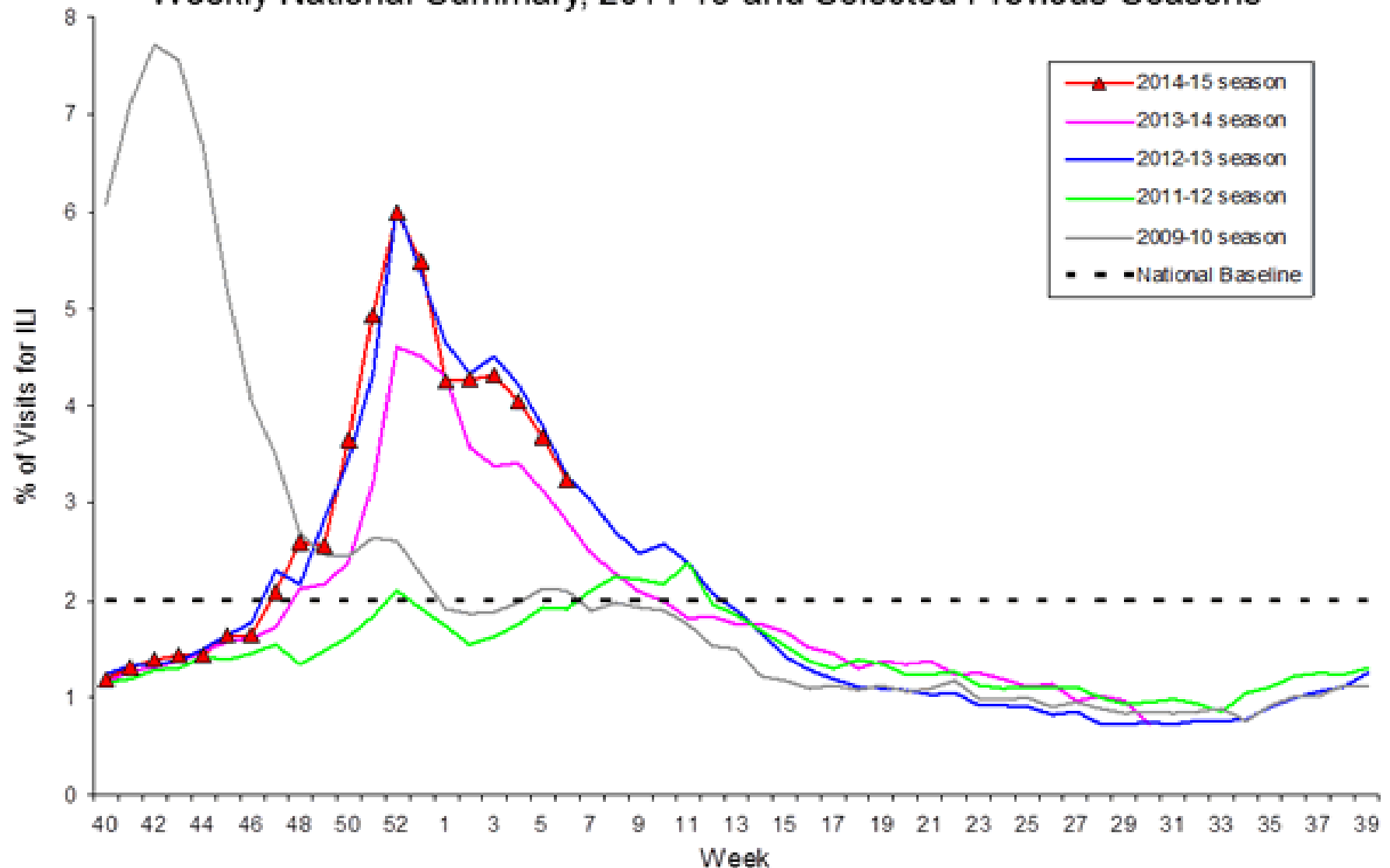


^a *MMWR*. 2010; 59(22):1057–1062.

^b All-cause hospitalization and mortality associated with influenza virus infection.

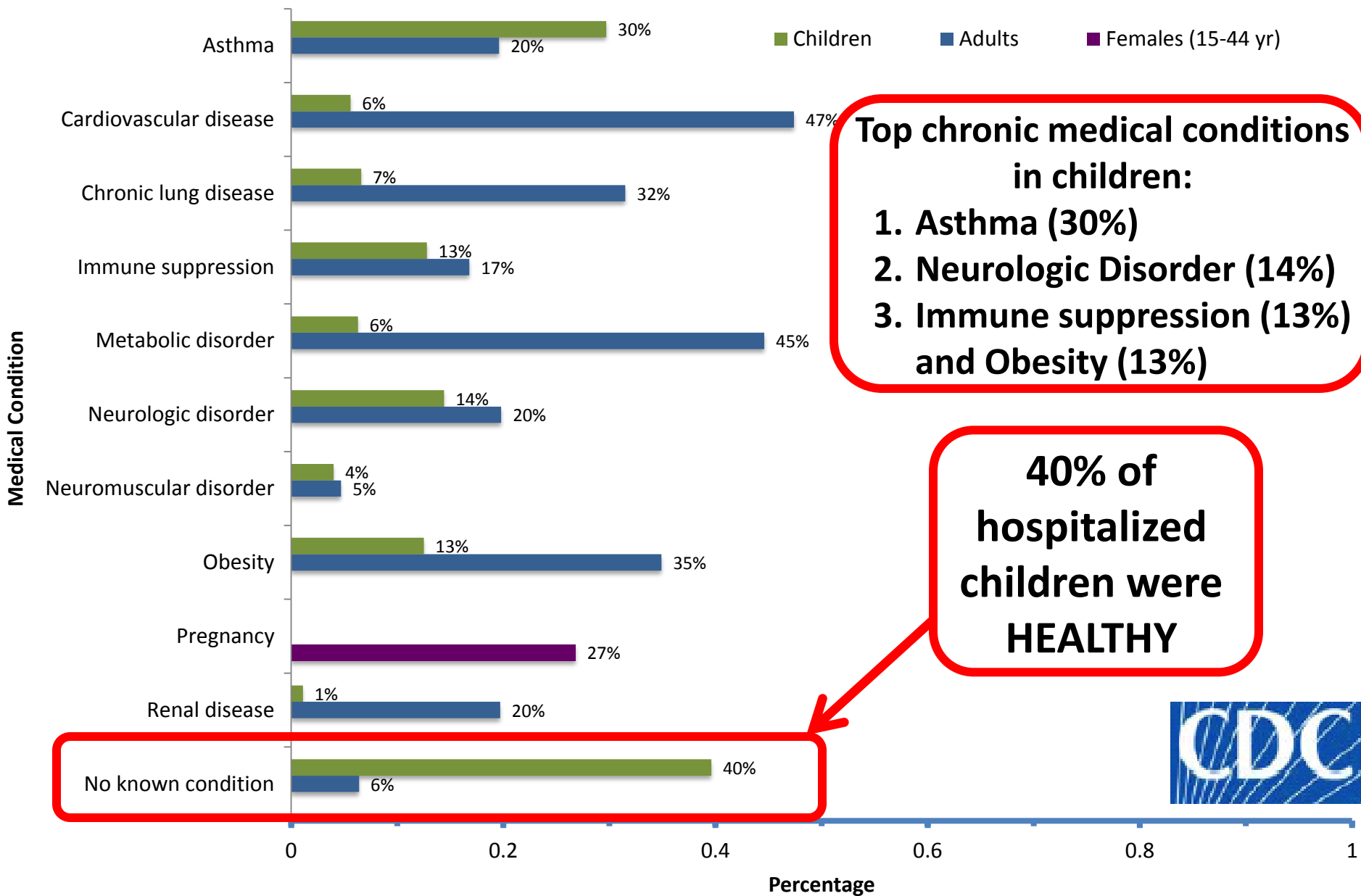
Thompson WW, et al. *JAMA*. 2003;289:179; Thompson WW, et al. *JAMA*. 2004;292:1333; Couch RB. *Ann Intern Med*. 2000;133:992; Patriarca PA. *JAMA*. 1999;282:75; ACIP. *MMWR*. 2004;53(RR06):1.

Percentage of Visits for Influenza-like Illness (ILI) Reported by the U.S. Outpatient Influenza-like Illness Surveillance Network (ILINet), Weekly National Summary, 2014-15 and Selected Previous Seasons

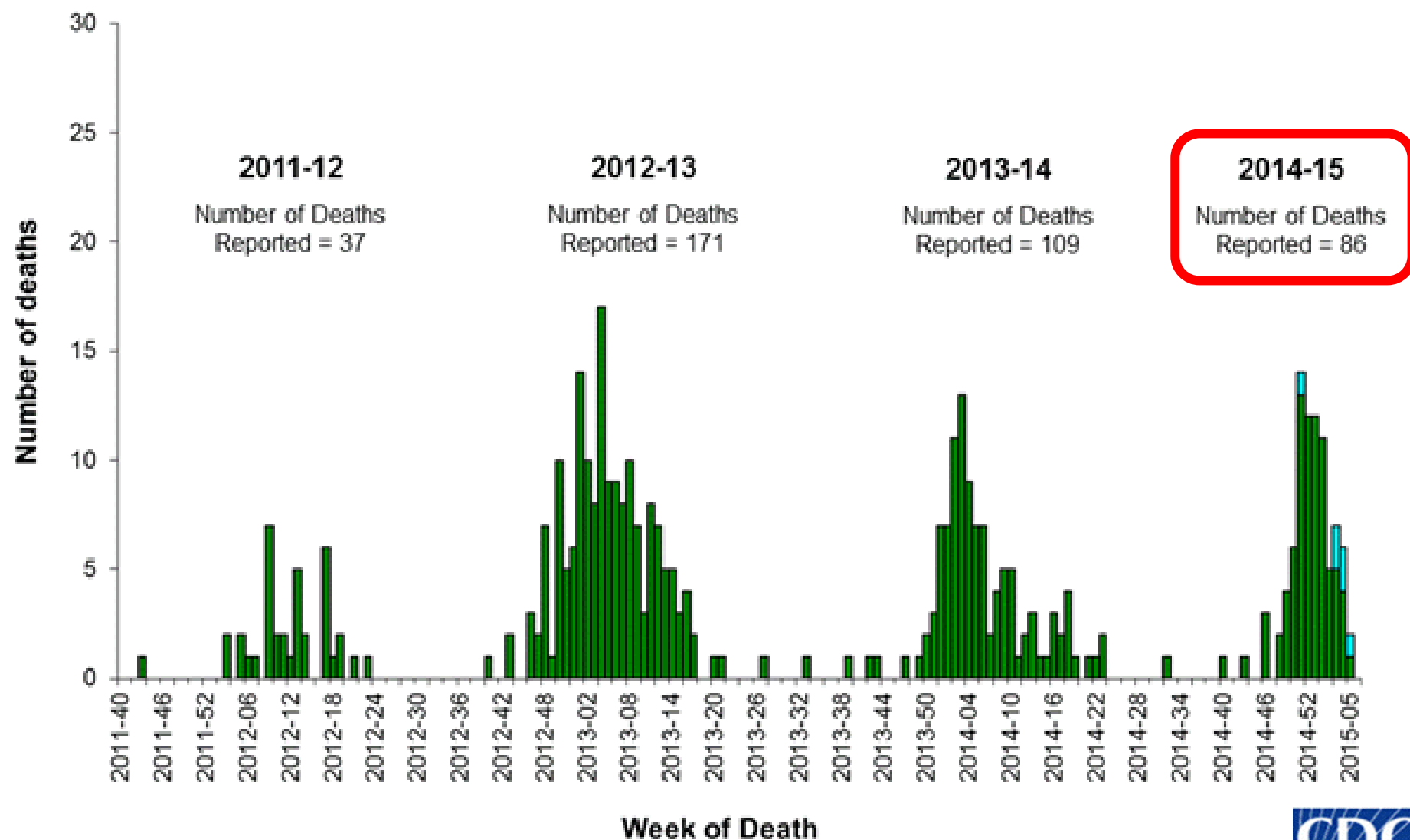


*There was no week 53 in the previous influenza seasons displayed above; therefore the week 53 data point for those seasons is an average of weeks 52 and 1.

Selected underlying medical conditions in patients hospitalized w/ influenza 2014-2015



Number of Influenza-Associated Pediatric Deaths by Week of Death: 2011-12 season to present



Pediatric Deaths and Hospitalizations By Season and Predominant Strain

Influenza Season	Predominant Strain	Pediatric Deaths	Hospitalizations (0-4 years old) per 100,000	Hospitalizations (5-17 years old) per 100,000
2014-2015* (preliminary data)	H3N2	86	43.4	12.4
2013-2014	pH1N1	109	47.3	9.4
2012-2013	H3N2	171	67	14.6
2011-2012*	H3N2	37	16	4
2010-2011	H3N2	123	49.5	9.1
2009-2010	pH1N1	288	77.4	27.2
2008-2009	H1N1	137	28	5
2007-2008	H3N2	88	40.3	5.5
2006-2007	H1N1	77	34.6	2.3
2005-2006	H3N2	46	28	4

*No change in vaccine strains from previous influenza season

2014-15 Seasonal Influenza Vaccine Strains

Trivalent

- A/California/7/2009 (H1N1)-like virus
- A/Texas/50/2012 (H3N2) virus
- B/Massachusetts/2/2012-like virus (B/Yamagata lineage)

Quadrivalent

- Adds B/Brisbane/60/2008-like virus (B/Victoria lineage)

All strains are unchanged from last season

	H1N1-like strain	H3N2-like strain	B-like strain
1986-'87	A/Chile/1/83 and A/Singapore/6/86	A/Christchurch/4/85-A/Mississippi/1/85	B/Ann Arbor/1/86
1987-'88	A/Singapore/6/86	A/Leningrad/360/1986	B/Ann Arbor/1/86
1988-'89	A/Singapore/6/86	A/Sichuan/2/87	B/Beijing/1/87
1989-'90	A/Singapore/6/86	A/Shanghai/11/87	B/Yamagata/16/88
1990-'91	A/Singapore/6/86	A/Guizhou/54/89	B/Yamagata/16/88
1991-'92	A/Singapore/6/86	A/Bangkok/1/89	B/Yamagata/16/88
1992-'93*	A/Singapore/6/86	A/Bangkok/1/89	B/Yamagata/16/88
1993-'94	A/Singapore/6/86	A/Bangkok/1/89	B/Yamagata/16/88
1994-'95	A/Singapore/6/86	A/Bangkok/1/89	B/Yamagata/16/88
1995-'96	A/Singapore/6/86	A/Bangkok/1/89	B/Yamagata/16/88
1996-'97	A/Singapore/6/86	A/Bangkok/1/89	B/Yamagata/16/88
1997-'98	A/Singapore/6/86	A/Bangkok/1/89	B/Yamagata/16/88
1998-'99	A/Singapore/6/86	A/Bangkok/1/89	B/Yamagata/16/88
1999-2000*	A/Singapore/6/86	A/Bangkok/1/89	B/Beijing/184/93
2000-'01	A/Singapore/6/86	A/Bangkok/1/89	B/Beijing/184/93
2001-'02	A/Singapore/6/86	A/Moscow/10/99	B/Sichuan/379/99
2002-'03	A/Singapore/6/86	A/Moscow/10/99	B/Hong Kong/330/2001
2003-'04*	A/New /20/99	A/Moscow/10/99	B/Hong Kong/330/2001
2004-'05	A/New /20/99	A/Fujian/411/2002	B/Shanghai/361/2002
2005-'06	A/New /20/99	A/California/7/2004	B/Shanghai/361/2002
2006-'07	A/New /20/99	A/Wisconsin/67/2005	B/Malaysia/2506/2004
2007-'08	A/Solomon Islands/3/2006	A/Wisconsin/67/2005	B/Malaysia/2506/2004
2008-'09	A/Brisbane/59/2007	A/Brisbane/10/2007	B/Florida/4/2006
2009-'10	A/Brisbane/59/2007	A/Brisbane/10/2007	B/Brisbane/60/2008
Pandemic	A/California/07/2009	A/California/07/2009	A/California/07/2009
2010-'11	A/California/07/2009	A/Perth/16/2009	B/Brisbane/60/2008
2011-'12*	A/California/07/2009	A/Perth/16/2009	B/Brisbane/60/2008
2012-'13	A/California/07/2009	A/Victoria/361/2011	B/Wisconsin/1/2010
2013-'14	A/California/07/2009	A/Texas/50/2012	B/Massachusetts/2/2012**
2014-'15*	A/California/07/2009	A/Texas/50/2012	B/Massachusetts/2/2012**

**Influenza is unpredictable:
Only 5 times in past 29 years
have vaccine strains not
changed from previous season**

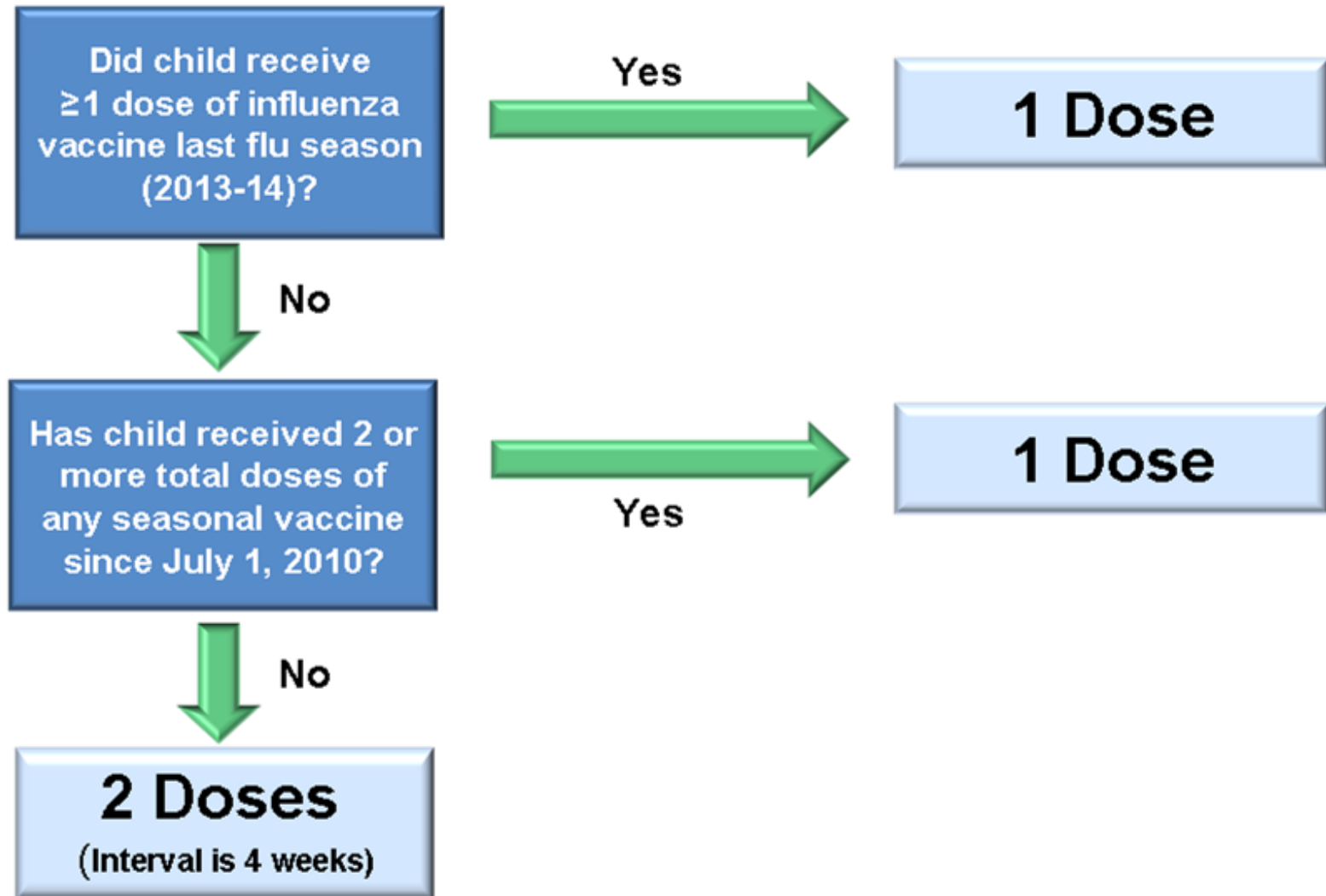
• No change in vaccine strains from previous season

** Quadrivalent vaccine with add'l B lineage available

**All people 6 months of age and older
should get flu vaccine every year**



Number of Seasonal Influenza Doses for Children 6 Months – 8 Years



LAIV or IIV?

- **Healthy children ages 2 through 8 years may be immunized with either IIV or LAIV (no preference)**
- **Vaccination should not be delayed to obtain a specific product**



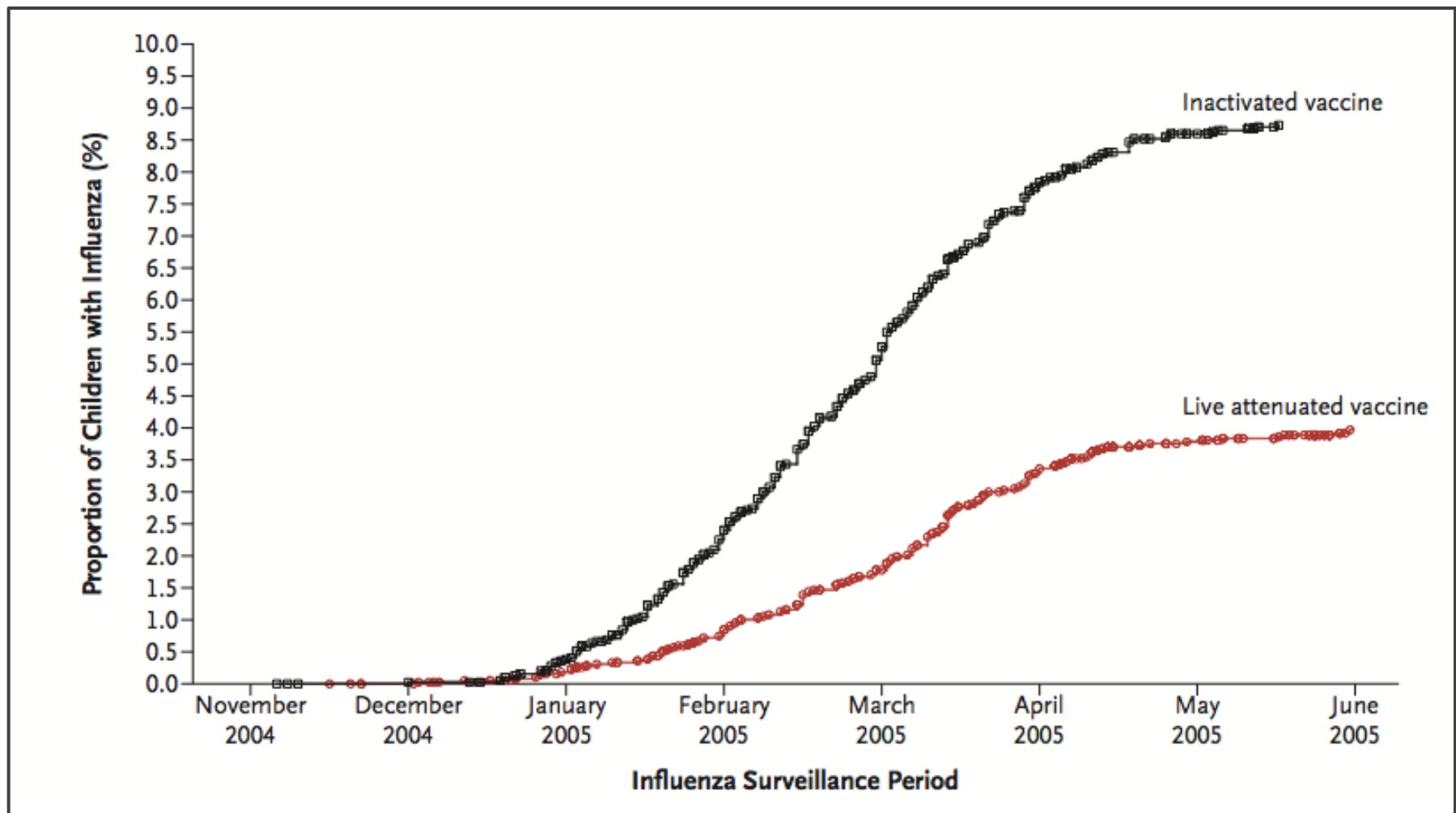
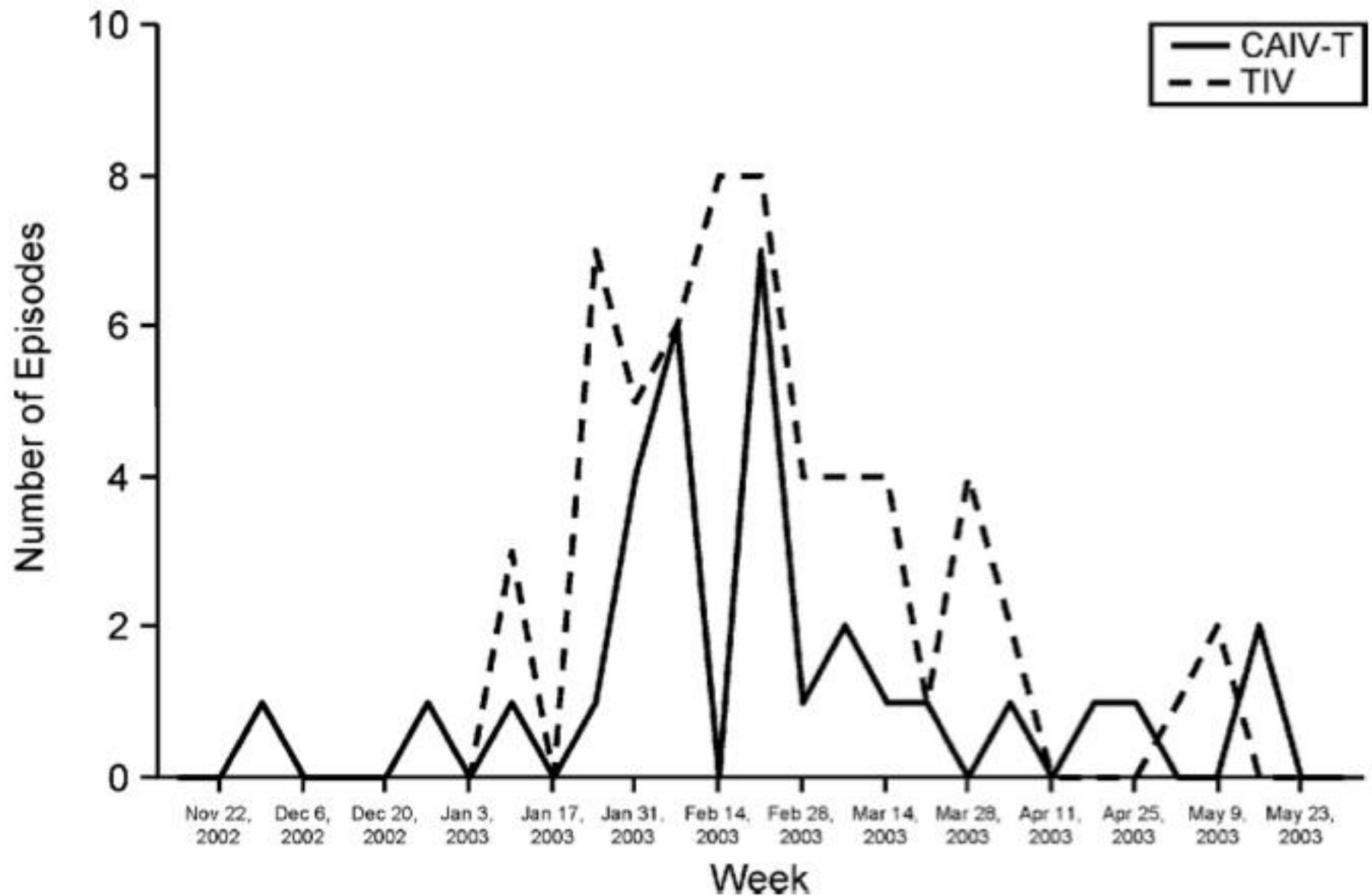


Figure 1. Kaplan–Meier Curves for the Time to the First Culture-Confirmed Report of Influenza in the Two Vaccine Groups.

Belshe RB, et al. Live attenuated versus inactivated influenza vaccine in infants and young children. *N Engl J Med*. 2007 Feb 15;356(7):685-96.



Ashkenazi S, et al. Superior relative efficacy of live attenuated influenza vaccine compared with inactivated influenza vaccine in young children with recurrent respiratory tract infections. *Pediatr Infect Dis J.* 2006 Oct;25(10):870-9.

LAIV Effectiveness (2013-2014)

- LAIV was not effective against influenza A pH1N1 pandemic virus when compared with IIV in children 2-8 years of age
- This contrasts with earlier GRADE analysis suggesting LAIV has superior efficacy in children 2-8 years of age
- AAP recommendation for LAIV changed from “to be considered” to “no preference”



"I hate it when we're not sure we're inoculating against the right strain of flu virus."

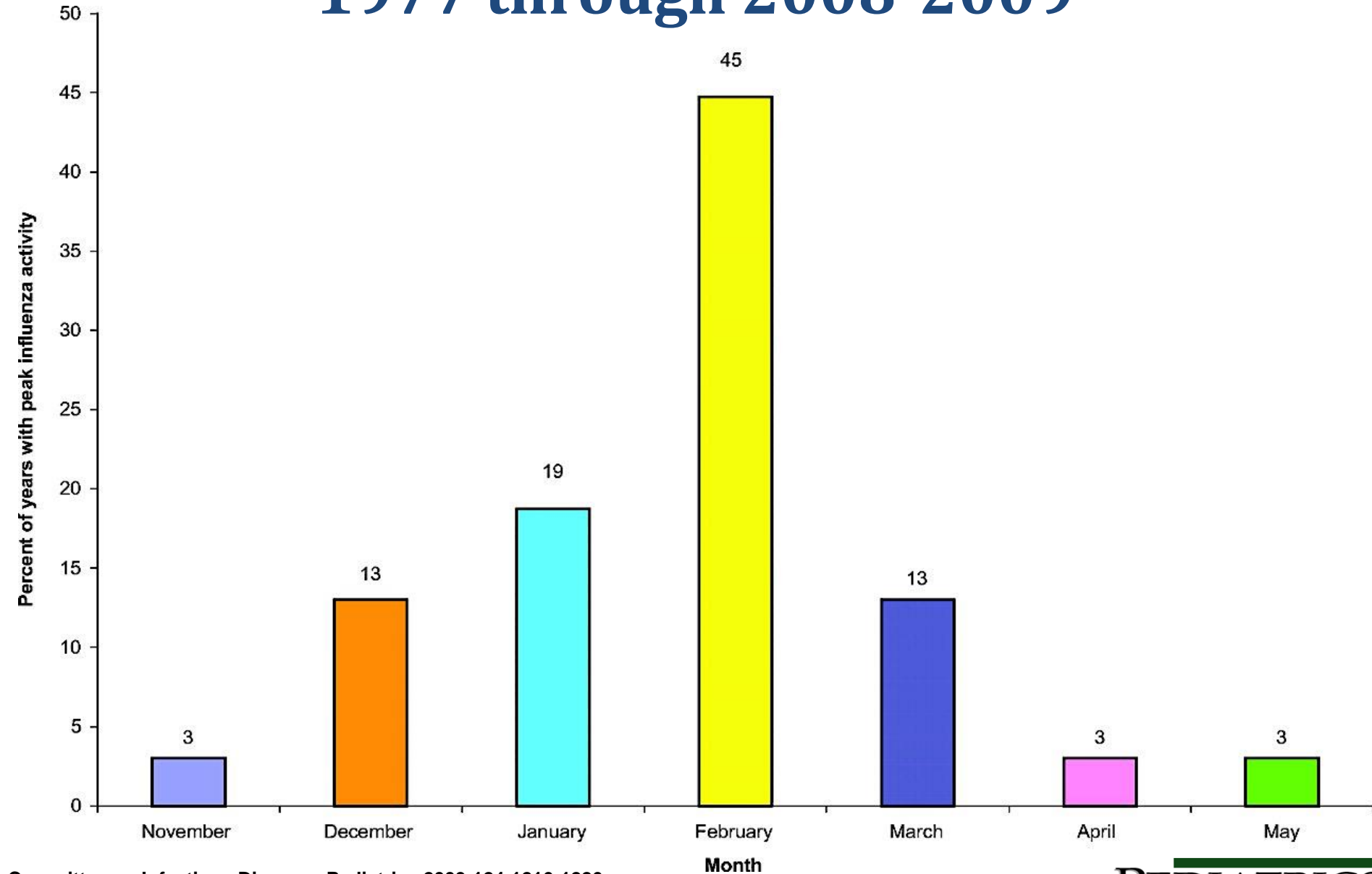
Vaccine Effectiveness

Influenza Season	Reference	No. of Patients	Age	Vaccine Type (LAIV or IIV)	VE % (95% CI)
2014-2015 Preliminary	ACIP 2015	1307 670	6 months – 8 years 9 years – 17 years	LAIV & IIV LAIV & IIV	23 (0–40) 17 (-19–42)
2013-2014	ACIP 2014	224 227	2 – 18 years 2 – 18 years	LAIV IIV	-5 (0–35) 60 (30–75)
2012-2013	McLean 2014	1509 981	6 months – 8 years 9 – 17 years	LAIV & IIV LAIV & IIV	57 (45–67) 39 (18–54)
2011-2012	Ohmit 2014	658 456 945 588	2 – 8 years 9 – 17 years 2 – 8 years 9 – 17 years	LAIV LAIV IIV IIV	61 (16–82) 60 (-15–86) 40 (6–62) 61 (28–79)
2010-2011	Treanor 2011	757 1116	2 – 8 years 2 – 8 years	LAIV IIV	71 (50–83) 71 (58–78)
2009-2010	Griffin 2011	1307 2020	2 – 9 years 6 months – 9 years	LAIV IIV	82 (14–96) 16 (-108–66)

VE against any flu by vaccine type, among 2-8 years (2014-2015)

	Influenza Positive		Influenza Negative					
	N vaccinated/Total I	(%)	N vaccinated/Total	(%)	Unadjusted VE	95% CI	Adjusted VE	95% CI
IIV vs. Unvaccinated	84/262	(32)	233/578	(40)	30%	(5, 49)	22%	(-8, 44)
LAIV vs. Unvaccinated	58/236	(25)	101/446	(23)	-6%	(-27, 12)	-18%	(-77, 22)

Month of Peak Influenza Activity from 1976-1977 through 2008-2009



Offer Vaccine Throughout Year

August 14

M	T	W	Th	F	Sa	S
4	5					
11	12					
18	19	20	21	22	23	24
25	26	27	28	29	30	31

September 14

M	T	W	Th	F	Sa	S
22	23	24	25	26	27	28
29	30					

October 14

M	T	W	Th	F	Sa	S
23	24	25	26	27	28	29
30	31					

November 14

M	T	W	Th	F	Sa	S
10	11	12	13	14	15	16
17	18	19	20	21	22	23
24	25	26	27	28	29	30

Start as soon as available

December 14

M	T	W	Th	F	Sa	S
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30	31				

January 15

M	T	W	Th	F	Sa	S
			1	2	3	4
5	6	7	8	9	10	11
12	13	14	15	16	17	18
19	20	21	22	23	24	25
26	27	28	29	30	31	

February 15

M	T	W	Th	F	Sa	S
2	3	4	5	6	7	8
9	10	11	12	13	14	15
16	17	18	19	20	21	22
23	24	25	26	27	28	

March 15

M	T	W	Th	F	Sa	S
30	31					1
2	3	4	5	6	7	8
9	10	11	12	13	14	15
16	17	18	19	20	21	22
23	24	25	26	27	28	29

April 15

M	T	W	Th	F	Sa	S
		1	2	3	4	5
6	7	8	9	10	11	12
13	14	15	16	17	18	19
20	21	22	23	24	25	26
27	28	29	30			

May 15

M	T	W	Th	F	Sa	S
				1	2	3
25	26	27	28	29	30	31

June 15

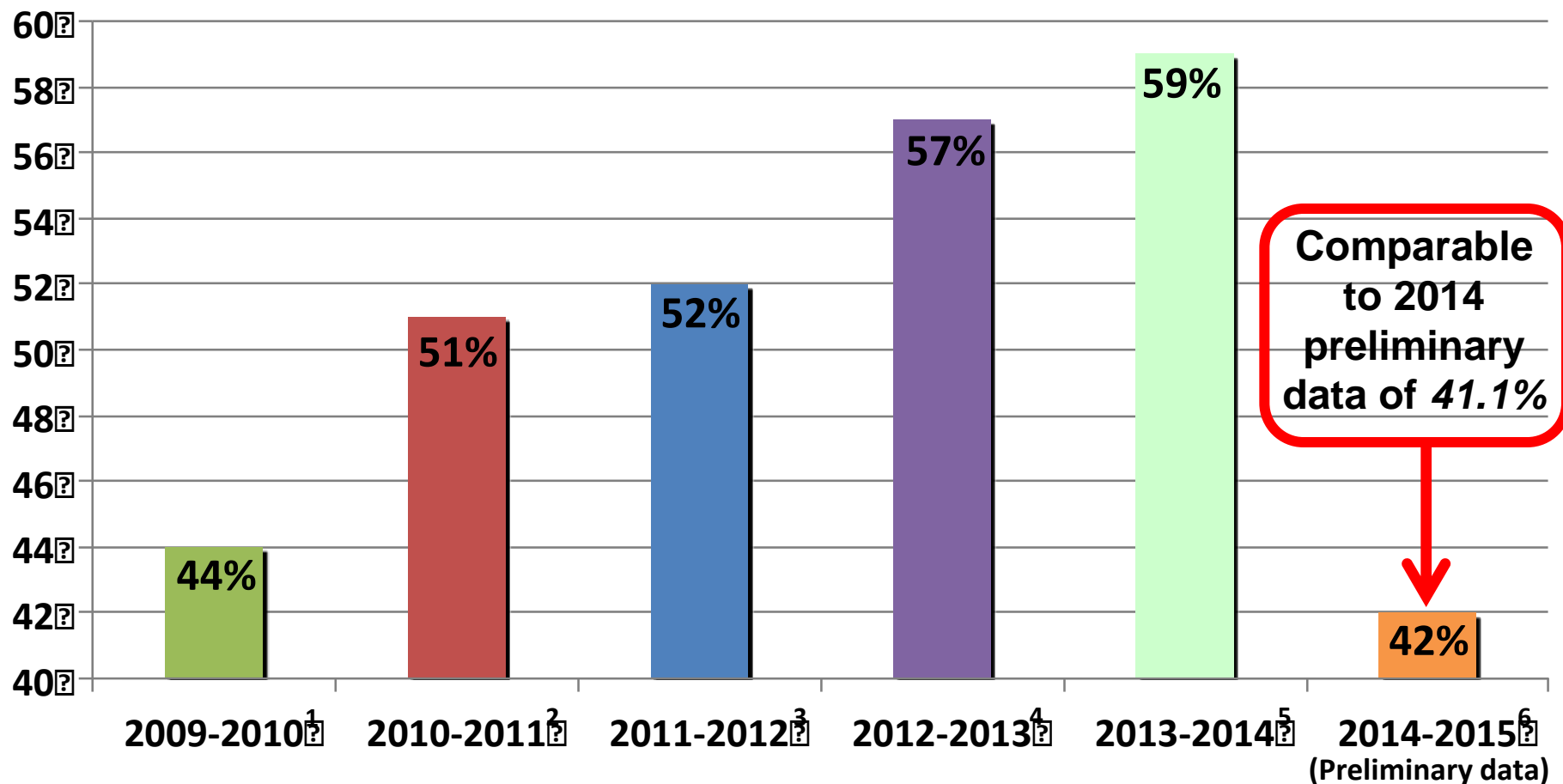
M	T	W	Th	F	Sa	S
1	2	3	4	5	6	7
8	9	10	11	12	13	14
15	16	17	18	19	20	21
22	23	24	25	26	27	28
29	30					

July 15

M	T	W	Th	F	Sa	S
		1	2	3	4	5
6	7	8	9	10	11	12
13	14	15	16	17	18	19
20	21	22	23	24	25	26
27	28	29	30	31		

Continue into late spring

Influenza Vaccine Coverage for Children 6 Months to 17 Years



¹ BRFSS and National 2009 H1N1 Flu Survey estimates, 2009–10. Online at: http://www.cdc.gov/flu/professionals/vaccination/coverage_0910estimates.htm.

² BRFSS and NIS estimates, 2010–11. Online at: http://www.cdc.gov/flu/professionals/vaccination/coverage_1011estimates.htm.

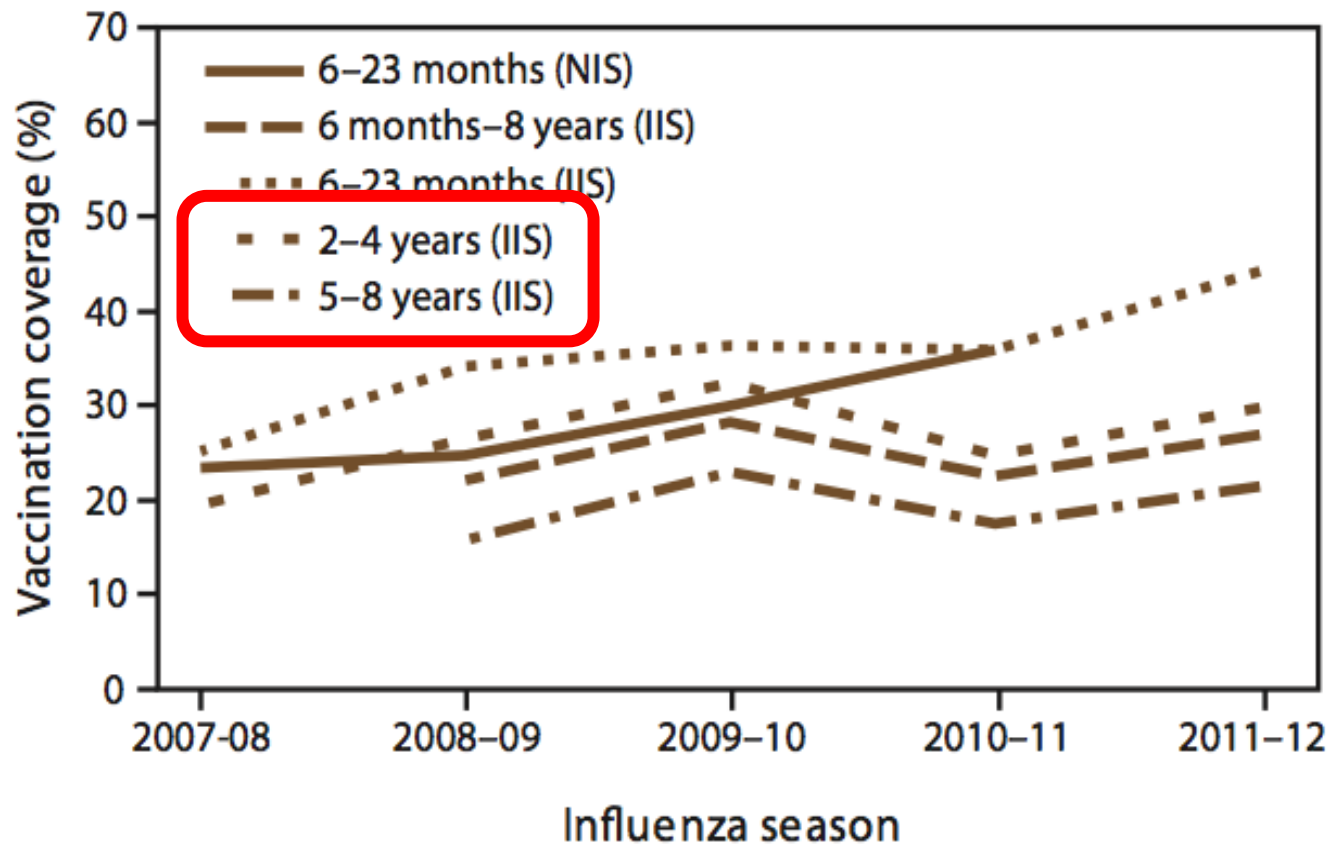
³ NIS estimates, 2011–2012. Online at http://www.cdc.gov/flu/professionals/vaccination/coverage_1112estimates.htm.

⁴ NIS estimates, 2012–2013. Online at <http://www.cdc.gov/flu/fluview/coverage-1213estimates.htm>

⁵ NIS estimates, 2012–2013. Online at <http://www.cdc.gov/flu/fluview/coverage-1314estimates.htm>

⁶ NIS estimates, 2013–2014. Online at <http://www.cdc.gov/flu/fluview/nifs-estimates-nov2014.htm>

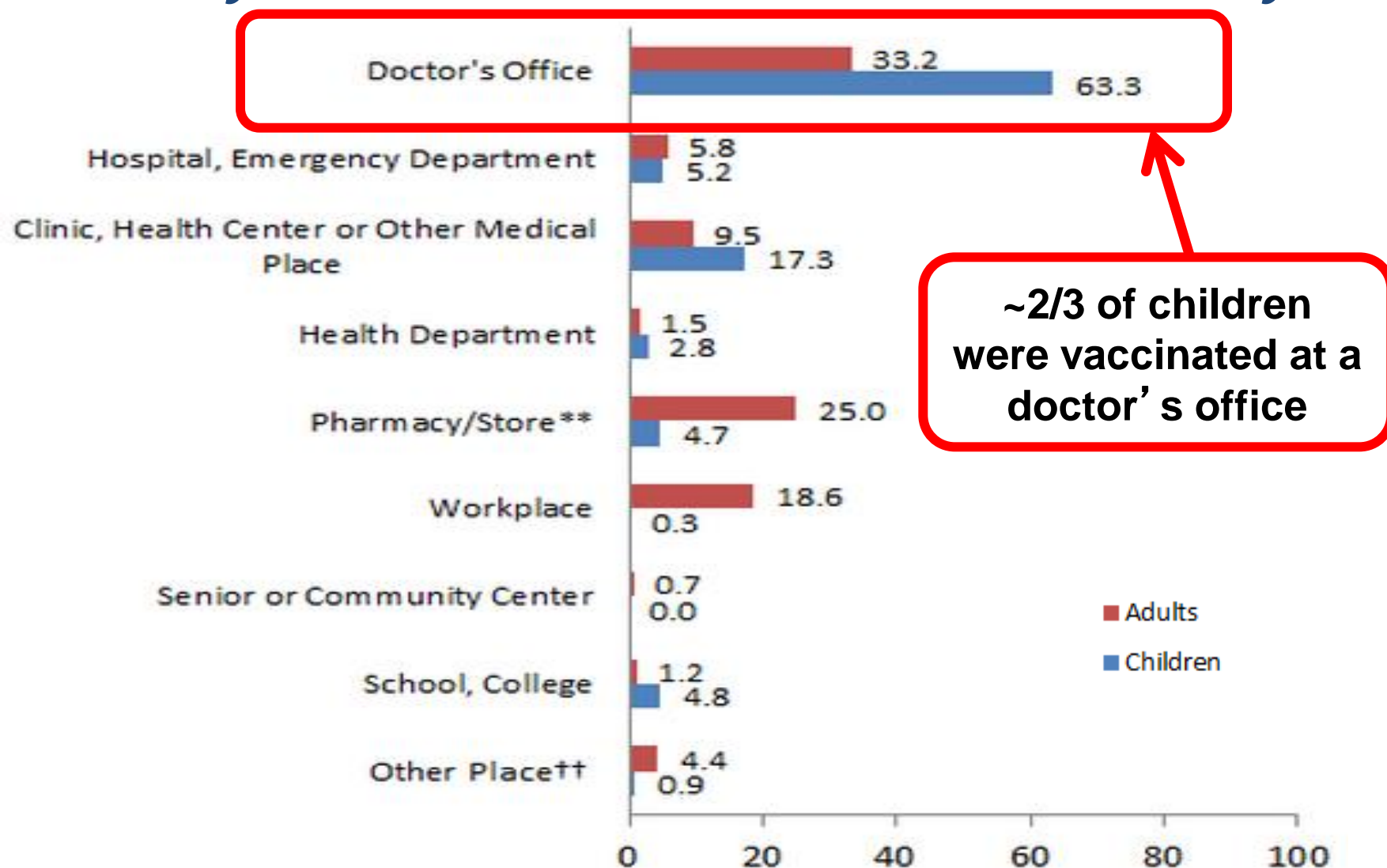
FIGURE 4. Full* influenza vaccination coverage among children aged 6 months–8 years — National Immunization Survey and Immunization Information System, United States, 2007–08 through 2011–12 influenza seasons†



Centers for Disease Control and Prevention (CDC). Surveillance of influenza vaccination coverage—United States, 2007–08 through 2011–12 influenza seasons. MMWR Surveill Summ. 2013 Oct25;62(4):1–28.

Place of Vaccination for Children and Adults

Early 2014-15 season, National Flu Survey



‡ includes hospitals, clinics or health centers, local health departments, and other.

Source: CDC. Available online at: <http://stacks.cdc.gov/view/cdc/26550>

Comparison of Types of Influenza Diagnostic Tests

Influenza Diagnostic Test	Method	Availability	Typical Processing Time	Sensitivity	Distinguishing Subtype Strains of Influenza A	Cost
Rapid influenza diagnostic tests (RIDTs)	Antigen detection	Wide	<15 minutes	10-70%	No	\$
Direct and indirect immunofluorescence assays (DFA and IFA)	Antigen detection	Wide	2-4 h	47-93%	No	\$
Tissue cell viral culture	Virus isolation	Limited	2-10 d	100%	Yes	\$\$
Nucleic acid amplification tests (including rRT-PCR)	RNA detection	Limited	2-4 d (6-8 h to perform test)	86-100%	Yes	\$\$\$
Rapid Influenza molecular assays	RNA detection	Wide	<15 minutes	86-100%	No	\$\$\$

Adapted from the Centers for Disease Control and Prevention (CDC) Guidance for clinicians on the use of rapid influenza diagnostic tests.
http://www.cdc.gov/flu/professionals/diagnosis/clinician_guidance_ridt.htm Accessed September 24, 2014.

Take Home Messages

- **Influenza H3N2 is the predominant strain; majority are drifted strains.**
- **Vaccine effectiveness may vary by match/mismatch of circulating virus with vaccine strains, vaccine product, and age of patient.**
- **Continue giving any licensed and age-appropriate influenza vaccine available; never delay for a specific product.**
- **Healthy children ages 2 through 8 years may be immunized with either IIV or LAIV (no preference).**

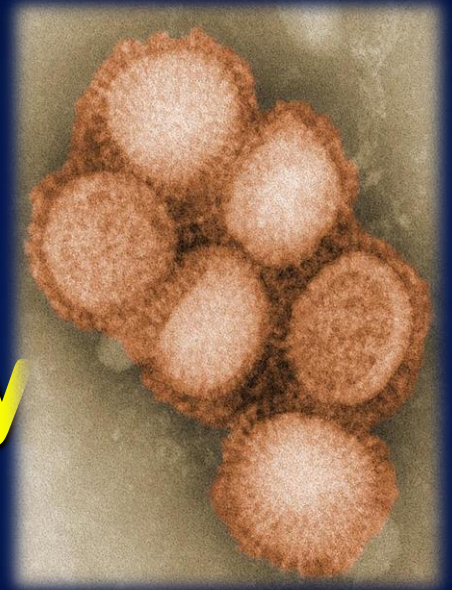
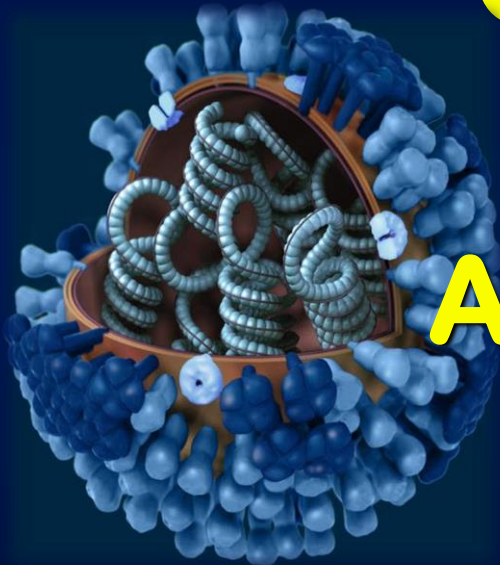
Pediatric Influenza

Clinician Outreach and Communication Activity

CDC with AAP

February 26, 2015

Antiviral Therapy



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Management of Influenza in Children

- Sources of information for pediatric practitioners on antivirals:
 - AAP Annual Influenza Guidance (published in the journal 'Pediatrics')
 - CDC (online at: <http://www.cdc.gov/features/flu-antivirals/>)
 - IDSA/PIDS Guidelines (currently under revision)

Management of Influenza in Children

AAP Committee on Infectious Diseases



POLICY STATEMENT

Recommendations for Prevention and Control of Influenza in Children, 2014–2015

COMMITTEE ON INFECTIOUS DISEASES

KEY WORDS

influenza, immunization, live attenuated influenza vaccine, inactivated influenza vaccine, vaccine, children, pediatrics

ABBREVIATIONS

AAP—American Academy of Pediatrics
ccIV3—trivalent cell culture-based inactivated influenza vaccine
CDC—Centers for Disease Control and Prevention
FDA—US Food and Drug Administration
GRADE—Grading of Recommendations Assessment, Development, and Evaluation
HCP—health care personnel
ID—intradermal
IIV—inactivated influenza vaccine
IIV3—trivalent inactivated influenza vaccine
IIV4—quadrivalent inactivated influenza vaccine
IM—intramuscular
LAIV—live attenuated influenza vaccine
LAIV4—quadrivalent live attenuated influenza vaccine
NAIs—neuraminidase inhibitors
PCR—polymerase chain reaction
PCV13—13-valent pneumococcal conjugate vaccine
pH1N1—influenza A (H1N1) pandemic virus
RIV3—trivalent recombinant influenza vaccine

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abstract

The purpose of this statement is to update recommendations for routine use of seasonal influenza vaccine and antiviral medications for the prevention and treatment of influenza in children. The American Academy of Pediatrics recommends annual seasonal influenza immunization for *all* people 6 months and older, including all children and adolescents. Highlights for the upcoming 2014–2015 season include the following:

1. The influenza vaccine composition for the 2014–2015 season is *unchanged* from the 2013–2014 season.
2. Both trivalent and quadrivalent influenza vaccines are available in the United States for the 2014–2015 season.
3. Annual universal influenza immunization is indicated with either a trivalent or quadrivalent vaccine (no preference).
4. Live attenuated influenza vaccine (LAIV) should be considered for *healthy* children 2 through 8 years of age who have no contraindications or precautions to the intranasal vaccine. If LAIV is not readily available, inactivated influenza vaccine (IIV) should be used; vaccination should not be delayed to obtain LAIV.
5. The dosing algorithm for administration of influenza vaccine to children 6 months through 8 years of age reflects that virus strains in the vaccine have not changed from last season.

As always, pediatricians, nurses, and all other health care personnel should be immunized themselves and should promote influenza vaccine use and infection control measures. **In addition, pediatricians should promptly identify clinical influenza infections to enable rapid antiviral treatment, when indicated, to reduce morbidity and mortality.**
Pediatrics 2014;134:1–17

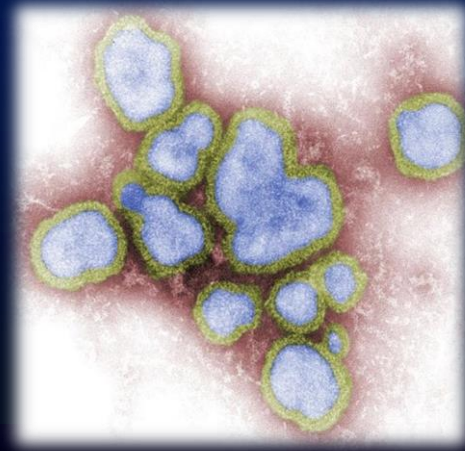
Management of Influenza 2014-15

- Problems with H3N2 this year: vaccine not well-matched with circulating strain
- CDC and AAP recommending early treatment of influenza disease with antivirals (regardless of immunization status this year)
- Circulating flu is susceptible to oseltamivir (Tamiflu®) and zanamivir (Relenza®)

CDC conducts ongoing testing for

Pediatric Populations at High Risk of Complications of Influenza (AAP/CDC)

- **Under 2 years (particularly under 6 months)**
- **Underlying comorbid condition**
 - Respiratory, Cardiovascular, Neurologic
- **Immunosuppression**
- **Pregnant or postpartum**
- **Native American populations**
- **Morbidly obese**



AAP (2014-5)

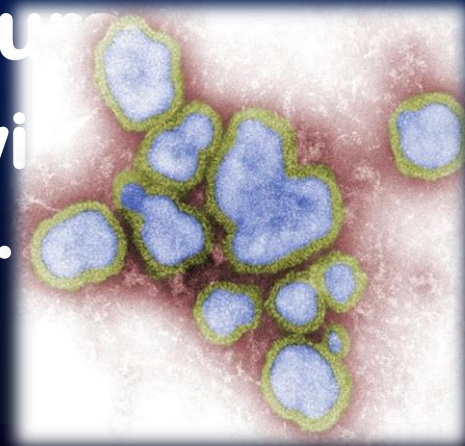
Treatment should be *offered* to:

- Influenza infection of any severity in children at high risk of complications
- Any child *hospitalized* with presumed influenza regardless of influenza immunization status or whether onset of illness occurred >48 hours before admission

AAP (2014-5)

Rx should be *considered* for

- Any otherwise healthy child with moderate to severe influenza disease
 - The greatest impact occurs with early treatment, but may still help for treatment started after 48 hours
 - We wish we could predict who will deteriorate and get hospitalized.



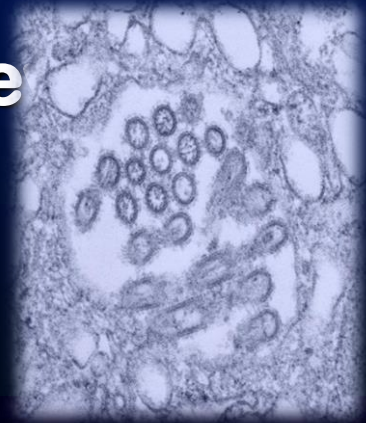
Duration of Illness Before Treatment

- The original FDA-approved clinical trial in pediatric outpatients specified no more than 48 hours of illness for healthy subjects
- No additional efficacy data from Roche or GSK have been presented to FDA re: longer periods of illness prior to treatment, or efficacy in high risk patients
- So the package label still says 48 hours

CDC: Antiviral Treatment

- “A negative rapid influenza antigen diagnostic test does not exclude influenza”

For clinical treatment decisions, rapid molecular tests and PCR are far more sensitive, but are more costly or take several hours to get results



Management of Influenza in Children

- Although risk of bacterial infection is increased with influenza infection, antibiotics are not routinely recommended
 - Treating early with antivirals can actually reduce the risk of bacterial superinfection

Antiviral Therapy

AAP Policy Statement 2014-15; Table 3

All you need to know about drugs and dosing is here!

TABLE 3 Recommended Dosage and Schedule of Influenza Antiviral Medications for Treatment and Chemoprophylaxis for the 2014–2015 Influenza Season: United States

Medication	Treatment (5 d)	Chemoprophylaxis (10 d)
Oseltamivir ^a		
Adults	75 mg twice daily	75 mg once daily
Children ≥ 12 mo		
Body wt		
≤ 15 kg (≤ 33 lb)	30 mg twice daily	30 mg once daily
> 15–23 kg (33–51 lb)	45 mg twice daily	45 mg once daily
> 23–40 kg (> 51–88 lb)	60 mg twice daily	60 mg once daily
> 40 kg (> 88 lb)	75 mg twice daily	75 mg once daily
Infants 9–11 mo ^b	3.5 mg/kg per dose twice daily	3.5 mg/kg per dose once daily
Term infants 0–8 mo ^b	3 mg/kg per dose twice daily	3 mg/kg per dose once daily for infants 3–8 mo; not recommended for infants < 3 mo, unless situation judged critical, because of limited safety and efficacy data in this age group
Preterm infants	See details in footnote ^c	
Zanamivir ^d		
Adults	10 mg (two 5-mg inhalations) twice daily	10 mg (two 5-mg inhalations) once daily
Children (≥ 7 y for treatment, ≥ 5 y for chemoprophylaxis)	10 mg (two 5-mg inhalations) twice daily	10 mg (two 5-mg inhalations) once daily

Management of Influenza in Children

- No national shortage of oseltamivir
- Local shortages of FDA-approved oseltamivir suspension may occur, but package label gives instructions for an extemporaneous suspension from the caps

IV Antivirals for Influenza

- **For infants who cannot tolerate oral oseltamivir or inhaled zanamivir, you might need to get some help from infectious disease specialists regarding the use of:**
- **Peramivir IV (Rapivab®)**
- **Zanamivir IV, for compassionate use**

Antiviral Treatment: Summary

1. Antiviral treatment should be started as soon as possible after illness onset for all of those hospitalized or in a high risk population
2. Consider treatment for otherwise healthy children with more severe infection caused by documented or highly suspected influenza, even after 48 hours of symptoms (but the earlier the better)



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- State your name
- Listen for the operator to call your name

Thank you for joining!
Please email us questions at coca@cdc.gov



Centers for Disease Control and Prevention
Atlanta, Georgia

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